

## IN THE CLAIMS

Please delete all prior lists of claims and insert the following list of claims:

1. (CURRENTLY AMENDED) An *in vitro* method of evaluating one or more test compounds to identify test compounds that modulate binding of ~~natural or artificial~~ regulatory factors to corresponding single-, double-, or triple-stranded nucleic acid binding sites, the method comprising:

(a) providing an isolated nucleic acid target that defines at least one known or putative binding site for a regulatory factor, the nucleic acid target having conjugated or covalently bonded thereto, at a point proximate to, but not within, the binding site:

- (i) an anchor moiety,
- (ii) a linker moiety covalently bonded to the anchor moiety, and
- (iii) a test compound bonded to the linker moiety; and then

(b) under transcription conditions, contacting *in vitro* the nucleic acid target of step (a) to a reagent mixture comprising one or more ~~natural or artificial~~ regulatory factors specific for the binding site defined in the nucleic acid target; and then

(c) determining whether binding of the regulatory factor to the binding site defined in the nucleic acid target is modulated by presence of the test compound.

2. (ORIGINAL) The method of Claim 1, wherein in step (a)(i), the anchor moiety comprises a polyamide or an intercalator.

3. (ORIGINAL) The method of Claim 1, wherein in step (a)(i), the anchor moiety comprises a moiety selected from the group consisting of a major-groove-binding/triple helix-forming oligonucleotide, a C<sub>1-6</sub> alkyl, a polycyclic aromatic hydrocarbon, a peptide nucleic acid, a polyamide, mitomycin C, cisplatin, and anthramycin.

4. (ORIGINAL) The method of Claim 1, wherein in step (a)(i), the anchor moiety is covalently bonded to the nucleic acid target.

5. (ORIGINAL) The method of Claim 1, wherein the isolated nucleic acid target defines one and only one known or putative binding site for a regulatory factor, and the nucleic acid target has conjugated or covalently bonded thereto one and only one anchor moiety.

6. (ORIGINAL) The method of Claim 5, wherein in step (a)(i), the anchor moiety comprises a moiety selected from the group consisting of a major-groove-binding/triple helix-forming oligonucleotide, a C<sub>1-6</sub> alkyl, a polycyclic aromatic hydrocarbon, an intercalator, a peptide nucleic acid, a polyamide, mitomycin C, cisplatin, and anthramycin.

7. (ORIGINAL) The method of Claim 5, wherein in step (a)(ii), the linker moiety comprises a bifunctional moiety selected from the group consisting of polypeptides, poly(ethyleneglycols), and C<sub>1-6</sub> alkylenyl, alkenyl, and alkynyl.

8. (ORIGINAL) The method of Claim 1, wherein in step (a)(ii), the linker moiety comprises a bifunctional moiety selected from the group consisting of polypeptides, poly(ethyleneglycols), and C<sub>1-6</sub> alkyl, alkene, and alkyne.

9. (ORIGINAL) The method of Claim 8, wherein in step (a)(i), the anchor moiety comprises a moiety selected from the group consisting of a major-groove-binding/triple helix-forming oligonucleotide, a C<sub>1-6</sub> alkyl, a polycyclic aromatic hydrocarbon, an intercalator, a peptide nucleic acid, a polyamide, mitomycin C, cisplatin, and anthramycin.

10. (ORIGINAL) The method of Claim 1, wherein in step (a)(ii), the linker moiety is an aptamer.

11. (ORIGINAL) The method of Claim 1, wherein in step (a)(ii), the linker moiety is at least 30 Å long.

12. (CURRENTLY AMENDED) ~~The method of Claim 1,~~ An *in vitro* method of evaluating one or more test compounds to identify test compounds that modulate binding

of regulatory factors to corresponding single-, double-, or triple-stranded nucleic acid binding sites, the method comprising:

(a) providing an isolated nucleic acid target that defines at least one known or putative binding site for a regulatory factor, the nucleic acid target having conjugated or covalently bonded thereto, at a point proximate to, but not within, the binding site:

(i) an anchor moiety,

(ii) a linker moiety covalently bonded to the anchor moiety, wherein in step (a)(ii), the linker moiety is entropically destabilized such that entropy of the linker moiety confers conditional behavior upon the isolated nucleic acid target, and

(iii) a test compound bonded to the linker moiety; and then

(b) under transcription conditions, contacting *in vitro* the nucleic acid target of step (a) to a reagent mixture comprising one or more regulatory factors specific for the binding site defined in the nucleic acid target; and then

(c) determining whether binding of the regulatory factor to the binding site defined in the nucleic acid target is modulated by presence of the test compound.

13. (ORIGINAL) A method of evaluating one or more test compounds to identify test compounds that facilitate, recruit, or stabilize binding of natural transcription factors to corresponding single-, double-, or triple-stranded transcription factor binding sites on nucleic acid, the method comprising:

(a) providing an isolated nucleic acid target that defines at least one desired transcription factor binding site, the nucleic acid target having covalently bonded thereto, at a point proximate to, but not within, the transcription factor binding site:

(i) an anchor moiety,

(ii) a linker moiety covalently bonded to the anchor moiety, and

(iii) a test compound bonded to the linker moiety; and then

(b) under transcription conditions, contacting *in vitro* the nucleic acid target of step (a) to a reagent mixture comprising one or more natural transcription factors specific for the transcription factor binding site defined in the nucleic acid target; and then

(c) determining whether the test compound alters binding of the natural transcription

factor to the nucleic acid target.

14. (ORIGINAL) The method of Claim 13, wherein the isolated nucleic acid target defines one and only one transcription factor binding site, and the nucleic acid target has covalently bonded thereto one and only one anchor moiety.

15. (ORIGINAL) The method of Claim 14, wherein in step (a)(i), the anchor moiety comprises a moiety selected from the group consisting of a major-groove-binding/triple helix-forming oligonucleotide, a C<sub>1-6</sub> alkyl, a polycyclic aromatic hydrocarbon, an intercalator, a peptide nucleic acid, a polyamide, mitomycin C, cisplatin, and anthramycin.

16. (ORIGINAL) The method of Claim 14, wherein in step (a)(ii), the linker moiety comprises a bifunctional moiety selected from the group consisting of polypeptides, poly(ethyleneglycols), and C<sub>1-6</sub> alkylenyl, alkenyl, and alkynyl.

17. (ORIGINAL) The method of Claim 13, wherein in step (a)(ii), the linker moiety comprises a bifunctional moiety selected from the group consisting of polypeptides, poly(ethyleneglycols), and C<sub>1-6</sub> alkyl, alkene, and alkyne.

18. (ORIGINAL) The method of Claim 17, wherein in step (a)(i), the anchor moiety comprises a moiety selected from the group consisting of a major-groove-binding/triple helix-forming oligonucleotide, a C<sub>1-6</sub> alkyl, a polycyclic aromatic hydrocarbon, an intercalator, a peptide nucleic acid, a polyamide, mitomycin C, cisplatin, and anthramycin.

19. (ORIGINAL) The method of Claim 13, wherein in step (a)(ii), the linker moiety is an aptamer.

20. (ORIGINAL) The method of Claim 13, wherein in step (a)(ii), the linker moiety is at least 30 Å long.

21. (CURRENTLY AMENDED) ~~The method of Claim 13,~~ A method of evaluating one or more test compounds to identify test compounds that facilitate, recruit, or stabilize binding of natural transcription factors to corresponding single-, double-, or triple-stranded transcription factor binding sites on nucleic acid, the method comprising:

- (a) providing an isolated nucleic acid target that defines at least one desired transcription factor binding site, the nucleic acid target having covalently bonded thereto, at a point proximate to, but not within, the transcription factor binding site:
  - (i) an anchor moiety,
  - (ii) a linker moiety covalently bonded to the anchor moiety, wherein ~~in step (a)(ii),~~ the linker moiety is entropically destabilized such that entropy of the linker moiety confers conditional behavior upon the isolated nucleic acid target, and
  - (iii) a test compound bonded to the linker moiety; and then
- (b) under transcription conditions, contacting *in vitro* the nucleic acid target of step (a) to a reagent mixture comprising one or more natural transcription factors specific for the transcription factor binding site defined in the nucleic acid target; and then
- (c) determining whether the test compound alters binding of the natural transcription factor to the nucleic acid target.

22. (CURRENTLY AMENDED) A method of evaluating one or more test compounds to identify test compounds that facilitate, recruit, or stabilize binding of **artificial** transcription factors to corresponding single-, double-, or triple-stranded transcription factor binding sites on nucleic acid, the method comprising:

- (a) providing an isolated nucleic acid target that defines at least one desired transcription factor binding site, the nucleic acid target having covalently bonded thereto, at a point proximate to, but not within, the transcription factor binding site:
  - (i) an anchor moiety,
  - (ii) a linker moiety covalently bonded to the anchor moiety, and
  - (iii) a test compound bonded to the linker moiety, wherein the test compound is known to modulate binding of natural transcription factors to the transcription factor binding site defined in the nucleic acid target; and then

(b) under transcription conditions, contacting *in vitro* the nucleic acid target of step (a) to a reagent mixture comprising one or more known or putative ~~artificial~~ transcription factors specific for the transcription factor binding site defined in the nucleic acid target; and then

(c) determining whether the test compound alters binding of the ~~artificial~~ transcription factor to the nucleic acid target.

23. (ORIGINAL) The method of Claim 22, wherein the isolated nucleic acid target defines one and only one transcription factor binding site, and the nucleic acid target has covalently bonded thereto one and only one anchor moiety.

24. (ORIGINAL) The method of Claim 23, wherein in step (a)(i), the anchor moiety comprises a moiety selected from the group consisting of a major-groove-binding/triple helix-forming oligonucleotide, a C<sub>1-6</sub> alkyl, a polycyclic aromatic hydrocarbon, an intercalator, a peptide nucleic acid, a polyamide, mitomycin C, cisplatin, and anthramycin.

25. (ORIGINAL) The method of Claim 23, wherein in step step (a)(ii), the linker moiety comprises a bifunctional moiety selected from the group consisting of polypeptides, poly(ethyleneglycols), and C<sub>1-6</sub> alkylenyl, alkenyl, and alkynyl.

26. (ORIGINAL) The method of Claim 22, wherein in step step (a)(ii), the linker moiety comprises a bifunctional moiety selected from the group consisting of polypeptides, poly(ethyleneglycols), and C<sub>1-6</sub> alkyl, alkene, and alkyne.

27. (ORIGINAL) The method of Claim 22, wherein in step (a)(i), the anchor moiety comprises a moiety selected from the group consisting of a major-groove-binding/triple helix-forming oligonucleotide, a C<sub>1-6</sub> alkyl, a polycyclic aromatic hydrocarbon, an intercalator, a peptide nucleic acid, a polyamide, mitomycin C, cisplatin, and anthramycin.

28. (ORIGINAL) The method of Claim 22, wherein in step (a)(ii), the linker moiety is an aptamer.

29. (ORIGINAL) The method of Claim 22, wherein in step (a)(ii), the linker moiety is at least 30 Å long.

30. (CURRENTLY AMENDED) ~~The method of Claim 22,~~ A method of evaluating one or more test compounds to identify test compounds that facilitate, recruit, or stabilize binding of transcription factors to corresponding single-, double-, or triple-stranded transcription factor binding sites on nucleic acid, the method comprising:

(a) providing an isolated nucleic acid target that defines at least one desired transcription factor binding site, the nucleic acid target having covalently bonded thereto, at a point proximate to, but not within, the transcription factor binding site:

(i) an anchor moiety,

(ii) a linker moiety covalently bonded to the anchor moiety, wherein in step (a)(ii), the linker moiety is entropically destabilized such that entropy of the linker moiety confers conditional behavior upon the isolated nucleic acid target, and

(iii) a test compound bonded to the linker moiety, wherein the test compound is known to modulate binding of natural transcription factors to the transcription factor binding site defined in the nucleic acid target; and then

(b) under transcription conditions, contacting *in vitro* the nucleic acid target of step (a) to a reagent mixture comprising one or more known or putative transcription factors specific for the transcription factor binding site defined in the nucleic acid target; and then

(c) determining whether the test compound alters binding of the transcription factor to the nucleic acid target.

31. (CURRENTLY AMENDED) A composition of matter comprising an isolated nucleic acid target that defines a desired or putative binding site for a regulatory factor, the isolated nucleic acid target having covalently bonded thereto, at a point proximate to the binding site, but not within the binding site, an anchor moiety, a linker moiety covalently bonded to the anchor moiety, and a test compound conjugated to the linker moiety.

32. (CURRENTLY AMENDED) The ~~method~~ composition of matter of Claim 31, wherein ~~in step (a)(ii)~~, the linker moiety is an aptamer.

33. (CURRENTLY AMENDED) The ~~method~~ composition of matter of Claim 31, wherein ~~in step (a)(ii)~~, the linker moiety is at least 30 Å long.

34. (CURRENTLY AMENDED) ~~The method of Claim 31,~~ A composition of matter comprising an isolated nucleic acid target that defines a desired or putative binding site for a regulatory factor, the isolated nucleic acid target having covalently bonded thereto, at a point proximate to the binding site an anchor moiety, a linker moiety covalently bonded to the anchor moiety, and a test compound conjugated to the linker moiety, wherein ~~in step (a)(ii)~~, the linker moiety is entropically destabilized such that entropy of the linker moiety confers conditional behavior upon the isolated nucleic acid target.

35. (CURRENTLY AMENDED) A kit for testing a compound for its ability to modulate binding of a regulatory factor to a corresponding regulatory factor binding site on a nucleic acid, the kit comprising:

an isolated nucleic acid target that defines a regulatory factor binding site, the isolated nucleic acid target further comprising an anchor moiety covalently bonded thereto at a point proximate to the regulatory factor binding site, but not within the regulatory factor binding site, and a bifunctional linker moiety covalently bonded to the anchor moiety, wherein the bifunctional linker moiety comprises a free terminus that is dimensioned and configured to be conjugated to a compound to be tested; the isolated nucleic acid target being disposed in a suitable container, and

instructions for use of the kit.

36. (CURRENTLY AMENDED) ~~The method of Claim 35,~~ A kit for testing a compound for its ability to modulate binding of a regulatory factor to a corresponding regulatory factor binding site on a nucleic acid, the kit comprising:



an isolated nucleic acid target that defines a regulatory factor binding site, the isolated nucleic acid target further comprising an anchor moiety covalently bonded thereto at a point proximate to the regulatory factor binding site, and a bifunctional linker moiety, wherein the bifunctional linker moiety is an aptamer, covalently bonded to the anchor moiety, wherein the bifunctional linker moiety comprises a free terminus that is dimensioned and configured to be conjugated to a compound to be tested; the isolated nucleic acid target being disposed in a suitable container, and  
instructions for use of the kit.

37. (ORIGINAL) The method of Claim 35, wherein the bifunctional linker moiety is at least 30 Å long.

38. (CURRENTLY AMENDED) ~~The method of Claim 35,~~ A kit for testing a compound for its ability to modulate binding of a regulatory factor to a corresponding regulatory factor binding site on a nucleic acid, the kit comprising:  
an isolated nucleic acid target that defines a regulatory factor binding site, the isolated nucleic acid target further comprising an anchor moiety covalently bonded thereto at a point proximate to the regulatory factor binding site, and a bifunctional linker moiety covalently bonded to the anchor moiety, wherein the bifunctional linker moiety is entropically destabilized such that entropy of the linker moiety confers conditional behavior upon the isolated nucleic acid target, and further wherein the bifunctional linker moiety comprises a free terminus that is dimensioned and configured to be conjugated to a compound to be tested; the isolated nucleic acid target being disposed in a suitable container, and  
instructions for use of the kit.